DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Memorandum

Date • APR - 7 1997

From Deputy Director, Clinical and Review Policy, Office of Device Evaluation (HFZ-400), Center for Devices and Radiological Health (CDRH)

Subject Premarket Approval of Medispec, Ltd.'s
Econolith™ Extracorporeal Shock Wave Lithotripter

To The Director, CDRH
ORA _____

ISSUE. Publication of a notice announcing approval of the subject PMA.

FACTS. Tab A contains a FEDERAL REGISTER notice announcing:

(1) a premarket approval order for the above referenced medical device (Tab B); and

(2) the availability of a summary of safety and effectiveness data for the device (Tab C).

RECOMMENDATION. I recommend that the notice be signed and published.

Kimber C. Richter
Kimber Richter, M.D.

Attachments
Tab A - Notice
Tab B - Order
Tab C - S & E Summary

DECISION

Approved X Disapproved _____ Date _____

Prepared by: Russell P. Pagano, Ph.D., CDRH, HFZ-470, 4-1-97, 594-2194

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food And Drug Administration

[DOCKET NO. _____]

Medispec, Ltd.; PREMARKET APPROVAL OF Econolith™ Lithotripter

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing its approval of the application by Medispec Ltd., Rockville, MD, for premarket approval, under the Federal Food, Drug, and Cosmetic Act (the act), of the Medispec Ltd. Econolith™ Lithotripter. FDA's Center for Devices and Radiological Health (CDRH) notified the applicant, by letter of April 7, 1997, of the approval of the application.

DATES: Petitions for administrative review by (insert date 30 days after date of publication in the FEDERAL REGISTER).

ADDRESSES: Written requests for copies of the summary of safety and effectiveness data and petitions for administrative review, to the Dockets Management Branch (HFA-305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1-23, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT:

Russell P. Pagano, Ph.D.,
Center for Devices and Radiological Health (HFZ-472),
Food and Drug Administration,
9200 Corporate Blvd.,
Rockville, MD 20850,
301-594-2194.

SUPPLEMENTARY INFORMATION: On December 26, 1995, Medispec Ltd., Rockville, MD, 20850, submitted to CDRH an application for premarket approval of the Econolith™ Lithotripter. The device is an extracorporeal shockwave lithotripter and is indicated for use in the noninvasive fragmentation of upper urinary tract stones between 5 and 20 millimeters in size.

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Gastroenterology and Urology Devices Panel of the Medical Devices Advisory Committee, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

On April 7, 1997, CDRH approved the application by a letter to the applicant from the Deputy Director of Clinical and Review Policy of the Office of Device Evaluation, CDRH.

A summary of the safety and effectiveness data on which CDRH based its approval is on file in the Dockets Management Branch (address above) and is available from that office upon written request. Requests should be identified with the name of the device and the docket number found in brackets in the heading of this document.

Opportunity for Administrative Review

Section 515(d)(3) of the act, (21 U.S.C. 360e(d)(3)) authorizes any interested person to petition, under section 515(g) of the act, for administrative review of CDRH's decision to approve this application. A petitioner may request either a

formal hearing under 21 CFR part 12 of FDA's administrative practices and procedures regulations or a review of the application and CDRH's action by an independent advisory committee of experts. A petition is to be in the form of a petition for reconsideration under 21 CFR 10.33(b). A petitioner shall identify the form of review requested (hearing or independent advisory committee) and shall submit with the petition supporting data and information showing that there is a genuine and substantial issue of material fact for resolution through administrative review. After reviewing the petition, FDA will decide whether to grant or deny the petition and will publish a notice of its decision in the FEDERAL REGISTER. If FDA grants the petition, the notice will state the issue to be reviewed, the form of the review to be used, the persons who may participate in the review, the time and place where the review will occur, and other details.

Petitioners may, at any time on or before (insert date 30 days after date of publication in the FEDERAL REGISTER), file with the Dockets Management Branch (address above) two copies of each petition and supporting data and information, identified with the name of the device and the docket number found in brackets in the heading of this document. Received petitions may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

This notice is issued under the Federal Food, Drug, and Cosmetic Act (secs. 515(d), 520(h), (21 U.S.C. 360e(d), 360j(h))) and under authority delegated to the Commissioner of Food and Drugs (21 CFR 5.10) and redelegated to the Director, Center for Devices and Radiological Health (21 CFR 5.53).

Dated:_____

_____

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

APR - 7 1997

Mr. Anil Dhingra
Chief Operating Officer
Medispec, Ltd. USA)
15200 Shady Grove Road
Suite 350
Rockville, Maryland 20850

Re: P950043
Econolith™ Extracorporeal Shock Wave Lithotripter
Filed: December 26, 1995
Amended: July 17, August 2, September 5, November 4 and 22, 1996;
and April 2, 1997

Dear Mr. Dhingra:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the Econolith™ Extracorporeal Shock Wave Lithotripter. This device is indicated for use in the non-invasive fragmentation of upper urinary tract stones between 5 and 20mm in size. We are pleased to inform you that the PMA is approved subject to the conditions described below and in the "Conditions of Approval" (enclosed). You may begin commercial distribution of the device upon receipt of this letter.

The sale, distribution, and use of this device are restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (the act) under the authority of section 515(d)(1)(B)(ii) of the act. FDA has also determined that to ensure the safe and effective use of the device that the device is further restricted within the meaning of section 520(e) under the authority of section 515(d)(1)(B)(ii), (1) insofar as the labeling specify the requirements that apply to the training of practitioners who may use the device as approved in this order and (2) insofar as the sale, distribution, and use must not violate sections 502(q) and (r) of the act.

In addition to the postapproval requirements in the enclosure, you have agreed to develop a protocol to collect long-term data to study the effect of your device on hypertension to fulfill the postapproval study requirements. The postapproval reports shall include a summary of your progress regarding the completion of the postapproval study requirements, including any available results.

CDRH will publish a notice of its decision to approve your PMA in the FEDERAL REGISTER. The notice will state that a summary of the safety and effectiveness data upon which the approval is based is available to the public upon request. Within 30 days of publication of the notice of approval in the FEDERAL REGISTER, any interested person may seek review of this decision by

requesting an opportunity for administrative review, either through a hearing or review by an independent advisory committee under section 515(g) of the act.

Failure to comply with the conditions of approval invalidates this approval order. Commercial distribution of a device that is not in compliance with these conditions is a violation of the act.

You are reminded that as soon as possible and before commercial distribution of your device, that you must submit an amendment to this PMA submission with copies of all approved labeling in final printed form.

All required documents should be submitted in triplicate, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

PMA Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Boulevard
Rockville, Maryland 20850

If you have any questions concerning this approval order, please contact Russell P. Pagano, Ph.D., at (301) 594-2194.

Sincerely yours,

Kimber C. Richter

Kimber Richter, M.D.
Deputy Director, Clinical
and Review Policy
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

CONDITIONS OF APPROVAL

APPROVED LABELING. As soon as possible, and before commercial distribution of your device, submit three copies of an amendment to this PMA submission with copies of all approved labeling in final printed form to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration (FDA), 9200 Corporate Blvd., Rockville, Maryland 20850.

ADVERTISEMENT No advertisement or other descriptive printed material issued by the applicant or private label distributor with respect to this device shall recommend or imply that the device may be used for any use that is not included in the FDA approved labeling for the device. If the FDA approval order has restricted the sale, distribution and use of the device to prescription use in accordance with 21 CFR 801.109 and specified that this restriction is being imposed in accordance with the provisions of section 520(e) of the act under the authority of section 515(d)(1)(B)(ii) of the act, all advertisements and other descriptive printed material issued by the applicant or distributor with respect to the device shall include a brief statement of the intended uses of the device and relevant warnings, precautions, side effects and contraindications

PREMARKET APPROVAL APPLICATION (PMA) SUPPLEMENT. Before making any change affecting the safety or effectiveness of the device, submit a PMA supplement for review and approval by FDA unless the change is of a type for which a "Special PMA Supplement-Changes Being Effected" is permitted under 21 CFR 814.39(d) or an alternate submission is permitted in accordance with 21 CFR 814.39(e). A PMA supplement or alternate submission shall comply with applicable requirements under 21 CFR 814.39 of the final rule for Premarket Approval of Medical Devices.

All situations which require a PMA supplement cannot be briefly summarized, please consult the PMA regulation for further guidance. The guidance provided below is only for several key instances.

A PMA supplement must be submitted when unanticipated adverse effects, increases in the incidence of anticipated adverse effects, or device failures necessitate a labeling, manufacturing, or device modification.

A PMA supplement must be submitted if the device is to be modified and the modified device should be subjected to animal or laboratory or clinical testing designed to determine if the modified device remains safe and effective.

A "Special PMA Supplement - Changes Being Effected" is limited to the labeling, quality control and manufacturing process changes specified under 21 CFR 814.39(d)(2). It allows for the addition of, but not the replacement of previously approved, quality control specifications and test methods. These changes may be implemented before FDA approval upon acknowledgment by FDA that the submission is being processed as a "Special PMA Supplement - Changes Being Effected." This acknowledgment is in addition to that issued by the PMA Document Mail Center for all PMA supplements submitted. This procedure is not applicable to changes in device design, composition, specifications, circuitry, software or energy source.

Alternate submissions permitted under 21 CFR 814.39(e) apply to changes that otherwise require approval of a PMA supplement before implementation of the change and include the use of a 30-day PMA supplement or annual postapproval report. FDA must have previously indicated in an advisory opinion to the affected industry or in correspondence with the applicant that the alternate submission is permitted for the change. Before such can occur, FDA and the PMA applicant(s) involved must agree upon any needed testing protocol, test results, reporting format, information to be reported, and the alternate submission to be used.

POSTAPPROVAL REPORTS. Continued approval of this PMA is contingent upon the submission of postapproval reports required under 21 CFR 814.84 at intervals of 1 year from the date of approval of the original PMA. Postapproval reports for supplements approved under the original PMA, if applicable, are to be included in the next and subsequent annual reports for the original PMA unless specified otherwise in the approval order for the PMA supplement. Two copies identified as "Annual Report" and bearing the applicable PMA reference number are to be submitted to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850. The postapproval report shall indicate the beginning and ending date of the period covered by the report and shall include the following information required by 21 CFR 814.84:

(1) Identification of changes described in 21 CFR 814.39(a) and changes required to be reported to FDA under 21 CFR 814.39(b).

(2) Bibliography and summary of the following information not previously submitted as part of the PMA and that is known to or reasonably should be known to the applicant:

(a) unpublished reports of data from any clinical investigations or nonclinical laboratory studies involving the device or related devices ("related" devices include devices which are the same or substantially similar to the applicant's device); and

(b) reports in the scientific literature concerning the device.

If, after reviewing the bibliography and summary, FDA concludes that agency review of one or more of the above reports is required, the applicant shall submit two copies of each identified report when so notified by FDA.

ADVERSE REACTION AND DEVICE DEFECT REPORTING. As provided by 21 CFR 814.82(a)(9), FDA has determined that in order to provide continued reasonable assurance of the safety and effectiveness of the device, the applicant shall submit 3 copies of a written report identified, as applicable, as an "Adverse Reaction Report" or "Device Defect Report" to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850 within 10 days after the applicant receives or has knowledge of information concerning:

(1) A mixup of the device or its labeling with another article.

(2) Any adverse reaction, side effect, injury, toxicity, or sensitivity reaction that is attributable to the device and

(a) has not been addressed by the device's labeling or

(b) has been addressed by the device's labeling, but is occurring with unexpected severity or frequency.

(3) Any significant chemical, physical or other change or deterioration in the device or any failure of the device to meet the specifications established in the approved PMA that could not cause or contribute to death or serious injury but are not correctable by adjustments or other maintenance procedures described in the approved labeling. The report shall include a discussion of the applicant's assessment of the change, deterioration or failure and any proposed or implemented corrective action by the applicant. When such events are correctable by adjustments or other maintenance procedures described in the approved labeling, all such events known to the applicant shall be included in the Annual Report described under "Postapproval Reports" above unless specified otherwise in the conditions of approval to this PMA. This postapproval report shall appropriately categorize these events and include the number of reported and otherwise known instances of each category during the reporting period. Additional information regarding the events discussed above shall be submitted by the applicant when determined by FDA to be necessary to provide continued reasonable assurance of the safety and effectiveness of the device for its intended use.

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REPORTING UNDER THE MEDICAL DEVICE REPORTING (MDR) REGULATION. The Medical Device Reporting (MDR) Regulation became effective on December 13, 1984, and requires that all manufacturers and importers of medical devices, including in vitro diagnostic devices, report to FDA whenever they receive or otherwise became aware of information that reasonably suggests that one of its marketed devices

(1) may have caused or contributed to a death or serious injury or

(2) has malfunctioned and that the device or any other device marketed by the manufacturer or importer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

The same events subject to reporting under the MDR Regulation may also be subject to the above "Adverse Reaction and Device Defect Reporting" requirements in the "Conditions of Approval" for this PMA. FDA has determined that such duplicative reporting is unnecessary. Whenever an event involving a device is subject to reporting under both the MDR Regulation and the "Conditions of Approval" for this PMA, you shall submit the appropriate reports required by the MDR Regulation and identified with the PMA reference number to the following office:

Division of Surveillance Systems (HFZ-531)
Center for Devices and Radiological Health
Food and Drug Administration
1350 Piccard Drive, Room 240
Rockville, Maryland 20850
Telephone (301) 594-2735

Events included in periodic reports to the PMA that have also been reported under the MDR Regulation must be so identified in the periodic report to the PMA to prevent duplicative entry into FDA information systems.

Copies of the MDR Regulation and an FDA publication entitled, "An Overview of the Medical Device Reporting Regulation," are available by written request to the address below or by telephoning 1-800-638-2041.

Division of Small Manufacturers Assistance (HFZ-220)
Center for Devices and Radiological Health
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

SUMMARY OF SAFETY AND EFFECTIVENESS DATA:
MEDISPEC ECONOLITH™ LITHOTRIPTER

I. GENERAL INFORMATION

DEVICE GENERIC NAME:	Extracorporeal Shock Wave Lithotripter
DEVICE TRADE NAME:	Econolith™ Lithotripter
APPLICANT:	Medispec Ltd. (USA) 15200 Shady Grove Road Suite 350 Rockville, MD 20850
PREMARKET APPROVAL APPLICATION (PMA) NUMBER:	P950043
DATE OF NOTICE OF APPROVAL TO THE APPLICANT:	APR - 7 1997

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II. INDICATIONS FOR USE

The Medispec Ltd.'s, Econolith™ Extracorporeal Shock Wave Lithotripter is indicated for use in the non-invasive fragmentation of upper urinary tract stones between 5 and 20mm in size.

III. DEVICE DESCRIPTION

The Medispec Ltd.'s, Econolith™ Lithotripter uses shock waves generated outside the patient's body to fragment urinary calculi within either the kidney or the upper ureter. The device consists of an electrohydraulic shock wave generator and control panel and a motorized patient table. Although the device does not provide imaging or monitoring functions, it does contain dedicated interfaces for the requisite fluoroscopic imaging and ECG monitoring. Specifications for compatible fluoroscopy and ECG units are provided in the labeling. A user-supplied respiration monitor may also be utilized.

The shockwave generator is a self-contained unit which includes an underwater electrode, a control system, a high voltage power supply, a focusing reflector, a water cushion, and a water supply system.

The treatment table is specifically designed for use with the Econolith™ Lithotripter. The table can position the patient in three dimensions and also provides access to the patient's lumbar region through removable inserts.

Stone Localization and Patient Positioning

The Econolith™ Lithotripter requires the ancillary use of a suitable C-arm X-ray device to localize the treated (targeted) stone at the appropriate focal point of the lithotripsy system. Prior to the patient entering the treatment room, the C-arm and the Econolith™ Lithotripter are aligned so that the center of rotation of the C-arm axis passes through the center of the focal point of the lithotripsy shock wave (f_2). The targeted stone is positioned at this focal point prior to shock wave treatment. The alignment procedure is performed using a removable focus pointer. The tip of this pointer corresponds to the location of f_2. During alignment, the C-arm is moved until the focus pointer

VB

tip is centered in the middle of a small, radiopaque "cross-hair" that corresponds to the center of the x-ray beam axis.

Once the alignment of the C-arm and Econolith™ Lithotripter is complete and verified, wheel clamps are locked to prevent inadvertent movement of either unit. Following this, the focus pointer is removed from the lithotripter and the treatment table (with patient) is moved into position.

The patient is then positioned using fluoroscopy and the table movement controls until the targeted stone remains at f_2 regardless of the orientation of the C-arm. Positioning is checked periodically during the treatment by imaging at two C-arm orientations and verifying that the target stone is still at f_2. Repositioning of the patient, as needed, can be performed during treatment to assure that the targeted stone is always at f_2.

Shock Wave Generation

The acoustic shock waves of the Econolith™ are generated when applied high voltage electrical energy produces a spark across the gap of an electrode positioned at one focus of a water-filled semi-ellipsoid reflector. The electrical discharge is synchronized to the R-wave of the patient's cardiac cycle. Vaporization of the water occurs at the location of the spark which produces spherical shockwaves. The shock waves generated then refocus at the second focal point of the ellipse. This focal point is the aforementioned f_2 where the targeted stone has been positioned.

IV. CONTRAINDICATIONS, WARNINGS, PRECAUTIONS

The labeling for the Econolith™ Lithotripter contains the following contraindications, warnings, and precautions:

Contraindications for the Econolith™ Lithotripter are:

1. Patients with a coagulation abnormality as indicated by abnormal prothrombin time (PT), partial thromboplastin time (PTT), or bleeding time, including patients receiving an anticoagulant (e.g., aspirin).

2. Patients with urinary tract obstructions distal to the

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target stone.

3. Patients in whom pregnancy is suspected.

4. Patients whose anatomy precludes focusing of the device in the area of the target stone, including obesity or severe curvature of the spine.

5. Patients with arterial calcification or vascular aneurysms in the lithotripter shock wave path.

6. Patients with a history of chronic or acute pancreatitis or gall bladder disease.

7. Patients whose weight exceeds the weight limit of the table (130 kg).

8. Patients in whom epidural or general anesthesia is contraindicated.

9. Patients in whom the use of x-ray is contraindicated.

Warnings for the Econolith™ Lithotripter are:

1. An imaging system is required in conjunction with the Econolith™ Lithotripter to locate the stone and to focus the shock wave on it. Do not operate the Econolith™ Lithotripter without an imaging system.

2. Although patients with infected stones and/or acute urinary tract infections have been successfully treated with shock wave therapy, the experience with the Econolith™ Lithotripter in such cases is limited. Therefore, the safety and effectiveness of treatment of infected stones with the Econolith™ Lithotripter have not been demonstrated. Due to the possibility of systemic infection from pathogen-bearing calculus debris, use of prophylactic antibiotics should be considered whenever the possibility of stone infection exists.

3. Bilateral treatment of renal stones should not be performed in a single treatment session because total

urinary tract obstruction by stone fragments may result. Patients with bilateral renal stones should be treated using a separate treatment session for each side. In the event of total urinary obstruction, corrective procedures may be needed to assure drainage of urine from the kidney.

4. Care should be taken to ensure that shock waves are not applied to air-filled areas, i.e., intestines or lungs. Shock waves are rapidly dispersed by passage through an air-filled interface which can cause harmful side effects.

5. Although children have been treated with shock wave therapy for upper urinary tract stones, experience with the Econolith™ Lithotripter in such cases is limited. Therefore, the safety and effectiveness of the Econolith™ Lithotripter in the treatment of urolithiasis in children have not been demonstrated. Studies indicate that there are growth plate disturbances in the epiphyses of developing long bones in rats subjected to shock waves. The significance of this finding in humans, however, is unknown.

6. The safety and effectiveness of using the Econolith™ Lithotripter in the treatment of middle and lower ureteral stones is currently unknown. The treatment of lower ureteral stones should specifically be avoided in women of childbearing age because treatment of this patient population could possibly result in irreversible damage to the female reproductive system and to the unborn fetus in an undiagnosed pregnancy.

Precautions for the Econolith™ Lithotripter are:

1. Cardiac monitoring should be performed during treatment. This is especially important for patients who may be at risk for cardiac arrhythmia due to a history of cardiac irregularities, because the use of extracorporeal shock wave lithotripsy is known to cause ventricular cardiac arrhythmias in some patients and limited information is available on the effect of the Econolith™ Lithotripter on cardiac rhythm.

2. Extreme caution must be used in the treatment of patients at high risk for heart failure, those with cardiac pacemakers or pneumonia, and patients with very low diaphragms. Although patients with implanted pacemakers have been treated with extracorporeal shock wave lithotripters[1], the safety of using the Econolith™ Lithitripter to treat patients with cardiac pacemakers and other implanted devices, whose function could be affected by shock waves, has not been studied.

3. Extracorporeal shock wave lithotripsy procedures have been known to cause damage to the treated kidney. The potential for injury, its long-term significance, and its duration are unknown. However, lithotripsy is believed to be less damaging than the persistence of the disease or alternative methods of treatment.

4. Treated patients should be followed radiographically until the patient is stone-free or there are no remaining stone fragments which are likely to cause a silent obstruction and loss of renal function.

5. While fluoroscopy must be used during the procedure, caution should be taken to minimize the exposure.

6. No safety and effectiveness information is available regarding the treatment of patients with staghorn calculi.

7. Experience treating impacted or embedded stones with the Econolith™ Lithotripter is limited and safety and effectiveness cannot be assured. Experience reported by other manufacturers and investigators using extracorporeal shock wave lithotripters for impacted stones has shown limited success. Alternative procedures are recommended.

8. It is recommended that there be no less than a 1 month interval between treatments of the same kidney or focal area, and no more than three treatments to the same kidney. The number of shock waves should be minimized and limited to 2,000 in a single treatment session.

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9. Patients should not be treated with the Econolith™ Lithotripter when the supervising urologist or the patient's primary care physician believes that the lithotripsy procedure or anesthesia is contraindicated by complicating conditions or the patient's poor health.

10. Due to noise associated with shock wave generation, both the patients and staff should wear ear protection during treatment.

V. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Adverse effects reported in association with the use of extracorporeal shock wave lithotripters include: skin bruising/redness at the treatment site, hematuria, renal colic/flank pain, nausea/vomiting, general/muscle pain, dysuria, elevated pancreatic amylase, infection, urosepsis, obstruction, renal hematomas, hypertension, hydronephrosis, and cardiac events. More detailed information on these events can be found on page 13 of this document.

VI. ALTERNATE PRACTICES AND PROCEDURES

Urinary tract stone treatment has been based predominantly on the symptomatology and location of the stone. Treatment varies with the type and size of stone and the condition of the patient. The most common treatment for kidney stones is dietary restriction and consumption of large amounts of fluid. Soft ammonium-magnesium phosphate and uric-acid calculi may be dissolved in some instances by irrigation through ureteral catheters. Calculi of small size may be removed from the lower ureter by means of instruments passed through the urethra into the ureter to snare the stone.

Patients with stones in the kidney and the proximal ureter with persistent and significant symptoms have historically been treated with open surgery, including partial nephrectomy and ureterolithotomy[2].

In recent years, percutaneous stone removal techniques have been developed for use on patients who were poor surgical candidates or had undergone open surgery in the past[3]. Percutaneous stone

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removal is now being used on patients who have not had previous operations because it is felt to be less invasive than open surgery and, in general, requires shorter hospitalization.

Other currently marketed extracorporeal shock wave lithotripters that have the same or broader indications for use offer another alternative.

VII. MARKETING HISTORY

A total of 165 Econolith™ Lithotripters have been sold in Europe, the Middle East, South and Central America, and Asia. No devices other than those in the study reported in this PMA have been sold in the United States. The 165 devices have been distributed under the name Econolith™ (95 devices), and Breakstone (70 devices). The device has not been withdrawn from marketing for any reason related to safety or effectiveness of the device.

VIII. SUMMARY OF STUDIES

1. NON-CLINICAL STUDIES

a. Evaluation of Shock Wave Pressure

Testing was conducted to characterize the shock wave generated by the Econolith™ Lithotripter. These tests were actually performed on the Breakstone version of the device, but the differences between these devices are minor and hardware related and the shock wave testing was determined to be valid for the Econolith™ Lithotripter. A polyvinylidene fluoride (PVDF) reference hydrophone capable of measuring rise times on the order of 20ns was used. The following data were collected.

Pressure Measurement Data		
Power Setting	Peak Positive Pressure (MPa)	Peak Negative Pressure (MPa)
16 kV	61	-8
20 kV	76	-9

In addition, integration of the energy per pulse was performed over the annular area within the -6 dB region around the point of peak pressure. The energy available was calculated to be 0.117J at 16kV and 0.140J at 20kV.

b. **Animal Study**

An animal study was conducted at Georgetown University Medical Center, Washington, D.C., using eight healthy dogs. The dogs were implanted with human calcium oxalate stones and subjected to 2,000 shocks at 20.5kV.

This study found that successful fragmentation of stones occurred in the animals with implanted human kidney stones. The tissue effects observed were mild to moderate in severity and transient. The results were consistent with reported literature on shock wave therapy in dogs.

2. CLINICAL INVESTIGATIONS

The clinical study performed in support of this application was performed at four investigational sites. The purpose of this investigation was to demonstrate the safety and effectiveness of the Econolith™ Lithotripter in the fragmentation of upper urinary tract calculi between 5mm and 20mm. A total of 211 treatments were administered to 180 patients. One hundred and eighty one patients were enrolled in the study, but one patient was never treated because of difficulties with the ECG gating procedure.

The 180 patients were treated for a total of 196 different stones. Safety and effectiveness data are reported on 174 patients (186 stones) in the total cohort. An evaluable cohort of 142 patients (150 stones) is also reported on for effectiveness. This cohort appropriately excludes patients treated early in the study at two of the sites. The excluded patients had statistically significantly lower success rates which led to a retraining of these investigators. Subsequent patients treated by these investigators had similar results to the patients treated at the other two sites. A training regimen has been developed by the company and will be required prior to use of the device. Despite the need for retraining at two of the four sites, the data collected were determined to be adequate to

evaluate safety and effectiveness.

The design of the clinical investigation of the Econolith™ Lithotripter is consistent with the recommendations that were made by the Gastroenterology and Urology Devices Panel members at their October 20, 1989, meeting. Specifically, the panel recommended that PMAs for renal extracorporeal shock wave lithotripters be based on a clinical study involving at least three investigational sites and 150 patients.

A list of the sites and investigators are presented in the following table.

Investigational Site	**Investigator**
Huguley Memorial Medical Center 11801 South Freeway Fort Worth, Texas 76115	John House, M.D.
Oneida City Hospital 321 Genesee Street Oneida, New York 13421	Bashar Omarbashar, M.D.
George H. Lanier Memorial Hospital 4800-48th Street Valley, Alabama 36854	Emiliano Saguier, M.D.
Southeast Missouri Hospital 1701 Lacey Street Cape Girardeau, Missouri 63701	Paul Thompson, M.D.

In all of the following discussions, the data are pooled and not separated into cohorts by investigational site. This was justified because after a series of analyses and the aforementioned retraining, there were no major differences in the results from the four sites.

a. <u>Subject Selection and Exclusion Criteria</u>

Patients eligible for inclusion in this study were adults who had upper urinary tract calculi with individual stone size >5mm and <21mm. There was no limit on the number of stones. Eligibility included being a candidate for an alternative surgical procedure for removal of the stone(s) and being in reasonably good health.

Exclusion criteria were as follows:

1. Patients whose anatomy prevented focusing of the device.

2. Patients with arterial calcification near the area to be treated.

3. Patients with urinary tract obstruction distal to the stone to be treated.

4. Patients in whom epidural or general anesthesia were contraindicated.

5. Patients in whom exposure to radiation was not advisable (e.g., suspected pregnancy).

6. Patients with a cardiac pacemaker.

7. Patients known to have struvite or cystine stones.

8. Patients with a coagulation abnormality or who were receiving drug therapy that may affect coagulation (e.g., aspirin).

Before enrollment in the study, patients were evaluated for suitability for lithotripsy. Information used in the evaluation included medical history and physical examination, laboratory work-up, and X-rays (including a KUB and intravenous pyelogram). Those patients who met the entrance criteria and signed an informed consent form were enrolled in the study.

b. Study Population

Of the 181 patients enrolled in the study, 121 (67%) were males and 60 (33%) were females. The mean age was 51 years (range 22 to 82 years) and the mean weight was 186 lbs. (range 113 to 296 lbs.).

The ratio of men to women in this study is similar to the ratios reported in similar studies, i.e., between 56% - 67% men and 33% - 44% women. The general patient population in this study is also comparable to the general populations reported in other studies, with similar demographic data reported for mean age, weight, etc.

c. **Stone Characteristics**

Of the 180 patients treated, 177 had stones >5mm and <21mm. Three of these patients are reported as still in follow-up and the remaining 174 patients account for the 186 treatments in the total cohort. The mean stone size was 9.2mm. Of the 186 targeted stones, 106 (57.0%) were located in calices, 35 (18.8%) were located in the renal pelvis, and 45 (24.2%) were located in the upper ureter. Seven of the ureter stones were pushed into the renal pelvis with a stent immediately prior to treatment.

d. **Treatment Characteristics**

The 180 patients treated received 211 procedures with an average number of shocks per treatment equal to 1936. The patients received an average of 4.5 minutes of fluoroscopy with the maximum output of the C-arms being less than 10 - 12 R/minutes. This level of radiation received by the patient does not present any safety issues. Over 98% of the patients received general anesthesia.

Retreatments

The criterion for retreatment was the presence of stones or fragments greater than 5mm in size. Of the 186 targeted stones, 16 were treated twice and 3 received three treatments. Based on the data from the above patients, the recommended retreatment schedule calls for a maximum of three treatments at a minimum interval of 1 month.

Ancillary Treatments

Stents were placed in approximately half of the patients. The placing of stents is standard medical practice; therefore, stenting is not considered a true ancillary treatment. Other procedures (percutaneous nephrostomy, balloon dilatation of the ureter, and basket extractions) were performed on 2.5% of the patients. These patients were considered lithotripsy failures.

e. **Results**

The effectiveness of treatment with the Econolith™ Lithotripter was evaluated by KUB to determine the presence and dimensions of remaining kidney stones or stone fragments after treatment. KUB's were performed immediately post-treatment and at subsequent follow-up

visits. Successful cases consisted of those patients who were stone free or had stone fragments less than or equal to 5mm in size at follow-up. The following table provides the effectiveness results of the study for the total and evaluable (post re-training) cohorts.

Success Rate

	Treated	Successes	% Success
Total Cohort	186	140	75.3%
Evaluable Cohort	150	125	83.3%
Non-Calyceal Stones	75	66	88.0%
Calyceal Stones	75	59	78.7%

The effects of selected patient characteristics on treatment outcome, including the average shock wave frequency, power level and number of shocks, age, sex, height, weight, BUN, creatinine, stone location and stone size, were analyzed. A significant difference was found indicating that stones located in the calyceal of the kidney could be expected to have a lower success rate. Since the rate for calyceal stones is acceptable in relation to other lithotripters, this difference is noted but not considered to be a serious adverse statement on the device's effectiveness. Stones larger than 10mm were also found to have a statistically lower success rate than smaller stones.

As stated earlier, after two of the sites received a retraining regimen, pooling of the results was justified. The pre-retraining patients are excluded from the evaluable cohort.

f. <u>Adverse Reactions and Complications</u>

Adverse effects reported in the study are similar to those reported for other lithotripters and are described below. The events are reported immediately post-treatment for all 211 procedures (this includes the retreatments), for the 174 patients in the total cohort at the 2 week visit following their last treatment, and for 76 patients seen at 3 months post-procedure. Patients were not followed to 3 months if they were classified as successes with no ongoing adverse events at a previous visit.

Adverse Event	Immediate post-op n=211	2 Weeks n=174	3 Months n=76
Bruising/Redness	160	13	0
Hematuria	144	24	4
Renal Colic/Flank Pain	63	15	5
Nausea/Vomiting	49	2	0
Muscle/General Pain	43	6	0
Dysuria	7	8	4
Elevated Pancreatic Amylase	5	6	0
UTI	2	7	1
Urosepsis	1	2	1
Perirenal Hematoma	1	1	0
Total Ureteral Obstruction	0	2	1
Sustained Arrhythmias	0		
Sustained Hypertension	10 (n=159)		

1. Bruising or redness at the treatment site was observed after 160 (75.8%) of the 211 treatments. No bruising or redness was reported at the 3 month visit.

2. Hematuria, defined as the presence of blood in the urine which can be seen with the naked eye, was observed after 144 (68.2%) of the 211 treatments, and in 4 out of 76 patients (5.3%) at the 3 month visit.

3. Renal Colic/Flank Pain, caused by distension of the ureter by a stone or stone fragment, was observed after 63 (29.9%) of the 211 treatments, and in 5 out of 76 patients (6.6%) at the 3 month visit.

4. Nausea and/or vomiting was experienced after 49 (23.2%) of the 211 treatments. No patients reported nausea and vomiting at the 3 month visit.

5. Muscle/general pain, defined as mild to moderate discomfort in the region of the shock wave entry was experienced after 43 (20.4%) of the 211 treatments. No patients had muscle or general pain at the 3 month visit.

6. Dysuria, defined as difficulty or pain on urination, was observed after 7 (3.3%) of the 211 treatments. Four patients (5.3%) experienced dysuria at the 3 month visit.

7. Elevated serum amylase levels, defined as an amylase level >3 standard deviations above the reference lab mean, were seen after 5 (2.4%) of the 211 treatments. No patients had elevated amylase levels at the 3 month visit.

8. Urinary Tract Infection (UTI), defined as a significant bacteriological contamination of the urinary tract, was seen after 2 (1.0%) of the 211 treatments. One patient (1.3%) had a urinary tract infection at the 3 month visit.

9. Urosepsis, defined as a spread of microorganisms into the blood from the urinary tract, was seen after 1 (0.5%) of the 211 treatments. One patient (1.3%) had urosepsis at the 3 month visit.

10. A perirenal hematoma extending from the left iliac crest to the mid-back region was observed after 1 treatment (0.5%). This case was conservatively managed and resolved without incident within 4 weeks.

11. Total Ureteral Obstruction, defined as complete

blockage of the ureter by a stone or stone fragment, was not experienced by any patients immediately post-treatment. One patient (1.3%) had a total ureteral obstruction at the 3 month visit.

12. Sustained arrhythmia, defined as a lasting change in the rhythm of the heart, was not observed in any of the patients.

13. Sustained hypertension, defined as an increase of ≥10mm Hg over pre-treatment levels at more than 1 follow-up visit, was observed in 10 (6.3%) of the 159 patients who had more than 1 follow-up visit.

g. Laboratory Values

Blood chemistries, hematology profiles, and urinalyses were performed on each patient at enrollment and at all follow-up visits. The only significant negative change in these laboratory values were the cases of elevated amylase reported in the adverse reaction section above.

h. Renal Scan

Renal scans and function assessments were performed on a subgroup of 31 patients. Due to administrative problems (e.g., patient did not receive a post-treatment scan), pre and post data exist on only 23 of these patients. Of these 23 patients, 95.6% (22/23) had either improved or stable renal function after treatment. The single abnormal patient had an elevated BUN/Creatinine level, but was judged improved by the radiologist. This case is not considered serious.

i. Device Failures

One device failure and one malfunction occurred during the study. These resulted in an aborted treatment and a 5 minute delay in a treatment. The aborted treatment was the result of a failure in the high voltage generator. The delayed treatment was caused by a water pump valve malfunction. No other device failures occurred during the study.

IX. CONCLUSIONS FROM THE STUDIES

The laboratory, animal, and clinical data provide reasonable assurance

of the safety and effectiveness of the Econolith™ Lithotripter for the non-invasive fragmentation of upper urinary tract stones between 5 and 20mm in size.

X. PANEL RECOMMENDATION

Pursuant to section 515(c)(2) of the Food, Drug, and Cosmetic Act (the act) as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Gastroenterology and Urology Devices Panel, an FDA advisory panel, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XI. CDRH DECISION

An FDA inspection of the Medispec, Ltd., (USA)., manufacturing facility was completed on December 4, 1996, and determined that the manufacturer was in compliance with the device Good Manufacturing Practices Regulation.

Based upon a review of the data contained in the PMA, CDRH determined that the Econolith™ Lithotripter is safe and effective for the indication of the non-invasive fragmentation of upper urinary tract stones between 5 and 20mm in size. Furthermore, the applicant agreed to the postapproval requirement that they design a study to collect data on the long-term effect of their device on hypertension.

CDRH issued an approval order for the stated indication for the applicant's PMA for the Medispec Econolith™ Lithotripter on APR - 7 1997.

XII. REFERENCES

1. Goldsmith M.F., "ESWL Now Possible for Patients with Pacemakers", JAMA, 258: pg. 1284, September 11, 1987.

2. Jameson R.M., Burrows K., Large B., Management of the Urological Patient, Churchill Livingston, New York: pp. 142-145, 1976.

3. Segura J.W, Patterson D.A., LeRoy A.J., May G.R., Smith L.H., "Percutaneous Lithotripsy," J. Urol., 130: pp. 1051-1054, 1983.

XIII. Approval Specifications

1. Instructions for Use: See labeling;
2. Hazards to Health from Use: See indications, contraindications, warnings, precautions, and adverse events sections of labeling;
3. Poatapproval Requirements and Restrictions: See approval order.

ECONOLITH™

OPERATING MANUAL

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April 1, 1997

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Appendices

INTRODUCTION

The Medispec ECONOLITH™ Lithotripter is indicated for use in the non-invasive fragmentation of upper urinary tract stones between 5 and 20 mm in size.

The ECONOLITH™ consists of a shock wave generator and a motorized treatment table.

The ECONOLITH™ Shock Wave Generator and Treatment Table are operated in conjunction with the following components (which are provided by the user):

1. Imaging System X-ray (C-Arm)
2. Electrocardiograph (ECG) Monitor
3. Respiration Sensor (if used)
4. Anesthetic Equipment (if used)

Caution: United States Federal law restricts this device to sale by or on the order of a licensed physician. It should be used only by qualified and trained personnel under the supervision of a physician.

Components of the ECONOLITH™ Lithotripter System

The ECONOLITH™ includes components for patient handling, patient positioning, and shock wave generation.

The components are:

1. The Shock Wave Generator (SWG), which includes:

    1.1 High voltage generator
    1.2 Control unit
    1.3 Water system
    1.4 Focusing reflector

2. Motorized 3-axis Treatment Table

    2.1 3-Axis motorized treatment table
    2.2 Hand-held remote control
    2.3 Detachable leg support
    2.4 Detachable mattress
    2.5 Cutout cover

3. Consumables

    3.1 Electrode
    3.2 Membrane

The ECONOLITH™ is to be operated in conjunction with an imaging system, an ECG monitor, and a respiration sensor (if used), which are not manufactured or supplied by MEDISPEC, LTD.

Clinical Information

2.1 Indications for Use

The Medispec ECONOLITH™ Lithotripter is indicated for use in the non-invasive fragmentation of upper urinary tract stones between 5 and 20 mm in size.

2.2 Contraindications to the use of the ECONOLITH™ Lithotripter

Use of the lithotripter is contraindicated under the following circumstances:

1. Patients with coagulation abnormalities as indicated by abnormal prothrombin time (PT), partial thromboplastin time (PTT), or bleeding time, including patients receiving an anticoagulant (e.g., aspirin).

2. Patients with urinary tract obstructions distal to the target stone.

3. Patients in whom pregnancy is suspected.

4. Patients whose anatomy precludes focusing of the device in the area of the target stone including obesity or severe curvature of the spine.

5. Patients with arterial calcification or vascular aneurysms in the lithotripter shock wave path.

6. Patients with a history of chronic or acute pancreatitis or gall bladder disease.

7. The patient's weight should not exceed the weight limit of the table (130 kg).

8. Patients in whom epidural or general anesthesia is contraindicated.

9. Any patient in whom the use of x-ray is contraindicated.

2.3 Warnings

1. An imaging system is required in conjunction with the Econolith™ Lithotripter to locate the stone and to focus the shock wave on it. Do <u>not</u> operate the Econolith™ Lithotripter without an imaging system.

2. Although patients with infected stones and/or acute urinary tract infections have been successfully treated with shock wave therapy, the experience with the Econolith™ Lithotripter in such cases is limited. Therefore, the safety and effectiveness of treatment of infected stones with the Econolith™ have not been demonstrated. Due to the possibility of systemic infection resulting from pathogen-bearing debris, use of prophylactic antibiotics should be considered whenever the possibility of stone infection exists.

3. Bilateral treatment of renal stones should not be performed in a single treatment session because total urinary tract obstruction by stone fragments may result. Patients with bilateral renal stones should be treated using a separate treatment session for each side. In the event of total urinary obstruction, corrective procedures may be needed to assure drainage of urine from the kidney.

4. Care should be taken to ensure that shock waves are not applied to air-filled areas, i.e., intestines or lungs. Shock waves are rapidly dispersed by passage through an air-filled interface which can cause harmful effects.

5. Although children have been treated with shock wave therapy for upper urinary tract stones, experience with the Econolith™ Lithotripter in this group is limited. Therefore, the safety and effectiveness of the Econolith™ in the treatment of urolithiasis in children have not been demonstrated. Studies indicate that there are growth plate disturbances in the epiphyses of developing long bones in rats subjected to shock waves. The significance of this finding in humans, however, is unknown.

6. The safety and effectiveness of use of the Econolith™ in the treatment of middle and lower ureteral stones is currently unknown. The treatment of lower ureteral stones should specifically be avoided in women in childbearing age because treatment of this patient population could possibly result in irreversible damage to the female reproductive system and to the unborn fetus in an undiagnosed pregnancy.

2.4 Precautions

1. Cardiac monitoring should be performed during treatment. This is especially important for patients who may be at risk for cardiac arrhythmia due to a history of cardiac irregularities, because the use of extracorporeal shock wave lithotripsy is known to cause ventricular cardiac arrhythmias in some patients, and limited information is available on the effect of the Econolith™ on cardiac rhythm.

2. Extreme caution must be used in the treatment of patients at high risk for heart failure. those with cardiac pacemakers or pneumonia, and patients with very low diaphragms. Although patients with implanted pacemakers have been treated with extracorporeal shock wave lithotripters,, the safety of using the Econolith™ to treat patients with cardiac pacemakers and other implanted devices whose function could be affected by shock waves has not been studied.

3. Extracorporeal shock wave lithotripsy procedures have been known to cause damage to the treated kidney. The potential for injury, its long-term significance, and its duration are unknown. However, lithotripsy is believed to be less damaging than the persistence of the disease or alternative methods of treatment.

4. Treated patients should be followed radiographically until the patient is stone-free or there are no remaining fragments which are likely to cause a silent obstruction and loss of renal function.

5. While fluoroscopy must be used during the procedure, caution should be taken to minimize the exposure.

6. No safety and effectiveness information is available regarding the treatment of patients with staghorn calculi.

7. Experience treating impacted or embedded stones with the Econolith™ Lithotripter is, limited and safety and effectiveness cannot be assured. Experience reported by other manufacturers and investigators using extracorporeal shock wave lithotripters for impacted stones has shown limited success. Alternative procedures are recommended.

8. It is recommended that there be no less than a one month interval between treatments of the same kidney or focal area, and no more than 3 treatments to the same kidney. The number of shock waves should be minimized and limited to 2,000 in a single treatment session.

9. Due to noise associated with shock wave generation, both the patients and staff should wear ear protection during treatment.

2.5 Clinical Study Synopsis

1. Study Design

Medispec Ltd. (USA) conducted a multi-site clinical trial to determine the safety and effectiveness of the Econolith™ Lithotripter in the non-invasive fragmentation of upper urinary tract calculi between 5 and 20 mm in size. These investigations were conducted at four sites in the United States, with a total of 181 patients.

The objective of the study was to determine the safety and success rates of fragmentation of stones treated with the ECONOLITH™ Lithotripter.

Radiologists evaluated the patient's radiographs for stone status, including size and location. The results were compared to those obtained in similar patients who underwent treatment with currently legally marketed lithotripters as reported in the literature.

Male or female patients older than 18 years of age with upper urinary tract stones were eligible for enrollment in the study. All patients were to have at least one stone greater than or equal to 5 mm and no stone larger than 20 mm; were to be classified as anesthesia risks I, II, III, or IV; were to have negative urine culture for bacteria; and were to have given informed consent.

Patients were excluded from the study if their anatomy prevented focusing of the device; if they had renal artery calcification in the treatment area; if they had lower or middle urinary tract stones or obstructions distal to the target stone; if epidural or general anesthesia was contraindicated; if exposure to radiation was not advisable (e.g., pregnancy); if they had a coagulation abnormality or were receiving drug therapy that may affect coagulation, including aspirin; if they had a cardiac pacemaker or other implanted device; or if they were known to have struvite or cystine stones.

A thorough history and physical examination was conducted prior to treatment. Follow-up tests, including anatomical and functional kidney evaluations, were performed on each patient at 2 weeks, 30 days, and 90 days following treatment or until the patient exited the study.

Success was defined as fragmentation of the targeted stone into pieces < 5 mm in their largest dimension. A patient could exit the study when he or she had completed the 90 day follow-up period or at any time it was determined that he/she was free of the target stone or had residual fragments of that stone measuring < 5 mm in diameter

2. Study Population

Of the 181 patients enrolled in the study, 121 were male and 60 were female. Patient age ranged from 22 to 82 years, with a mean of 51 years. Patient weight varied widely, ranging from 113 lbs. to 296 lbs. with a mean of 186 lbs. Of the 181 patients enrolled in this study, 47% had a history of kidney stone disease.

The treated stones ranged in size from 4 mm to 22 mm in largest diameter. However, data analysis was performed only on stones which were in the 5 to 20 mm range (186 targeted stones), as specified in the Indications for Use section. The mean stone size was 9.2 mm. Of the 186 targeted stones, 106 (57.0%) were located in the calices; 35 (18.8%) were located in the renal pelvis. Forty-five of the 186 target stones (24.2%) were originally located in the ureter, 7 of which were pushed into the renal pelvis with a stent immediately prior to treatment.

Of the 181 patients enrolled, 180 patients received 211 treatments. An average of 1936 shocks were delivered per treatment.

3. *Safety* The adverse effects in Table 1 below were observed during the study. The occurrence is cited for the total cohort[1] in the study.

[1] The total cohort consists of 174 patients who were treated with stone sizes in the evaluable range of 5-20 mm.

Table 1
Numbers of Adverse Events During the Clinical Study
(Immediate Post-Op n=Total # of Treatments; 2 Weeks & 3 Months Post-Op n=Total # of Patients at Visit)

Adverse Event	Immediate Post-Op (n=211 txs.)	2 Weeks Post-Op (n=174 pts.)	3 Months Post-Op (n=76 pts.)
Bruising/Redness	160	13	0
Hematuria	144	24	4
Renal Colic/Flank Pain	63	15	5
Nausea/Vomiting	49	2	0
Muscle/General Pain	43	6	0
Dysuria	7	8	4
Elevated Pancreatic Amylase	5	6	0
UTI	2	7	1
Urosepsis	1	2	1
Perirenal Hematoma	1	1	0
Total Ureteral Obstruction	0	2	1
Sustained Arrhythmias	0		
Sustained Hypertension	10 (n=159 pts.)		

i. Bruising or Redness at the treatment site, which has been reported by most of the manufacturers of lithotripsy devices was observed in 160 (75.8%) of the 211 treatments with the ECONOLITH™ immediately post-op. Bruising and redness had disappeared at the three month visit.

ii. Hematuria, defined as the presence of blood in the urine which can be seen with the naked eye, was observed in 144 (68.2%) of the 211 treatments with the ECONOLITH™ immediately post-op, and in 4 out of 76 patients (5.3%) at the three month visit.

iii. Renal Colic/Flank Pain, caused by distension of the ureter by a stone or stone fragment, was observed in 63 (29.9%) of the 211

treatments with the ECONOLITH™ immediately post-op, and in 5 out of 76 patients (6.6%) at the three month visit.

iv. Nausea and Vomiting, ranging from mild nausea to severe vomiting requiring hospitalization is a common adverse effect of lithotripsy. Of the 211 treatments Medispec ECONOLITH™, 49 (23.2%) experienced nausea and vomiting immediately post-op. No patients reported nausea and vomiting at the three month visit.

v. Muscle/General Pain, defined as mild to moderate discomfort in the region of the shock wave entry, was experienced by 43 (20.4%) of the 211 treatments with the ECONOLITH™ immediately post-op, and no patients had muscle pain at the three month visit.

vi. Dysuria, defined as difficulty or pain on urination, was observed in 7 (3.3%) of the 211 treatments with the ECONOLITH™ immediately post-op, and in 4 out of 76 patients (5.3%) at the three month visit.

vii. Elevated Pancreatic Amylase Levels, defined as a serum amylase level >3 S.D. above the reference lab mean, were seen in 5 out of 211 treatments (2.4%) immediately post-treatment. No patients had elevated amylase levels at the three month visit.

viii. Urinary Tract Infection (UTI), defined as a significant bacteriological contamination of the urinary tract, was seen in 2 (1.0%) of the 211 treatments with the ECONOLITH™ immediately post-op, and in 1 out of 76 patients (1.3%) at the three month visit.

ix. Urosepsis, defined as a spread of microorganisms into the blood from the urinary tract, was seen in 1 (0.5%) of the 211 treatments with the ECONOLITH™ immediately post-op, and in 1 out of 76 patients (1.3%) at the three month visit.

x. Perirenal Hematoma, defined as a retroperitoneal dissection of blood around the region of the kidney, was seen in 1 (0.5%) of the 211 treatments with the ECONOLITH™ immediately post-op. The hematoma resolved spontaneously within 4 weeks post-treatment without sequelae.

xi. Total Ureteral Obstruction, defined as complete blockage of the ureter by a stone or stone fragment, was not experienced by any of the 211 treatments with the ECONOLITH™ immediately post-op. One out of 76 patients (1.3%) had a total ureteral obstruction at the three month visit.

xii. Sustained arrhythmia, defined as a lasting change in the rhythm of the heart, was not observed in any of the patients treated with the Medispec ECONOLITH™

xiii. Sustained hypertension, defined as an increase of ≥ 10 mm Hg over pre-treatment levels at more than 1 follow-up visit, was observed in 10 (6.3%) of the 159 patients who had more than 1 follow-up visit.

4. Anesthesia Use During Treatment

Of the 211 treatments with the Medispec ECONOLITH™ during the clinical study, 208 (98.6%) were performed with general anesthesia, 2 (0.9%) were performed with intravenous (IV) sedation, and 1 (0.5%) was performed without anesthesia or analgesia.

5. Effectiveness

Evaluation of the effectiveness of treatment with the ECONOLITH™ Lithotripter was based on the presence and size of retained kidney stones or stone fragments 3 months post-treatment. The treatment was considered effective if one of the following criteria was met: (i) the patient was completely free of the targeted stone(s) at 3 months or less; or (ii) the patient retained no fragments from the targeted stone(s) that were 5 mm or larger in the upper urinary tract. The evaluable cohort (n = 150) excludes patients who were treated early in the study at two of the four sites These patents had lower success rates than the overall study population. Upon retraining of the investigators at these sites, the success rates for the subsequent cases were shown to be statistically poolable.

Table 2
Success (Effectiveness) Rates

Site	Targeted Stones	Successes	% Success
Total Cohort	186	140	75.3%
Evaluable Cohort	150	125	83.3%
Non-Calyceal Stones	75	66	88.0%
Calyceal Stones	75	59	78.7%